

Parkinson's Disease Information Sheet 1.7

MPTP and Drug-Induced Parkinson's

Idiopathic Parkinson's disease (Pd) is a progressive neurological condition which is characterised by motor (movement) and non-motor symptoms. Information Sheet 1.2 describes the major symptoms in detail.

Idiopathic Pd is characterised pathologically by the loss of dopamine producing neurons in the substantia nigra within the mid-brain. While this is not the only pathological feature of the condition it is evident in all cases at post mortem. Another major feature is the presence of Lewy bodies. These are concentric inclusion bodies which can be identified by using a red dye called eosin. They are considered a hallmark of Idiopathic Pd.

MPTP (1-methyl-4-phenyl-1,2,3,6-tetra/hydropyridine)

The cause of cell death in Idiopathic Pd is unknown however it is recognised that the neurotoxin MPTP is selectively toxic to the cells in the substantia nigra resulting in the signs and symptoms similar to Idiopathic Pd.

The first case of MPTP induced Parkinsonism occurred in 1976 when a college student manufacturing an illicit narcotic (MPPP) erroneously produced MPTP. Within three days of taking the narcotic he was severely Parkinsonian. Eventually he was commenced on and responded to levodopa therapy. Following his death (two years later) the autopsy showed cell destruction in the substantia nigra. The damage was identical to that seen in Idiopathic Pd except for the absence of Lewy bodies.

In 1982 batches of MPPP were again manufactured and sold in the street as synthetic heroin. Eventually contaminated batches containing MPTP hit the streets, which resulted in severe end stage Parkinsonian symptoms in users as young as 19. The source was traced to MPTP which caused permanent damage to the neurons of the substantia nigra resulting in the presentation of Pd. These

observations clearly indicated the anatomical location of the origin of the disease process that is Parkinson's.

MPTP-induced Parkinsonism has a fast progression (as rapid as a few days to full symptoms), whereas Idiopathic Pd has a slow progression from onset to end stages.

While patients with MPTP-induced Parkinsonism show all the clinical features of Pd, it is not Idiopathic Pd. MPTP-induced Parkinsonism is very selective, whereas with Idiopathic Pd other areas of the brain are affected. However, the MPTP model is useful in the laboratory setting and in the development of pharmacological treatments.

Dr J William Langston, a major researcher into MPTP, investigated the animal model and observed the effects of MPTP in the human model, resulting in a large body of knowledge on the effects and consequences of MPTP.

A vital discovery is that MPTP results in severe Parkinsonism in the primate model. Dr Langston observed that a monkey treated with oral doses of levodopa develops fluctuations in motor function as well as the 'wearing off' phenomenon. This led to his theory that since the laboratory animals had not been exposed to high doses of levodopa the complications which occur with levodopa therapy (such as dyskinesia and 'on-off' phenomena) may be more related to severity of disease than to duration of therapy.

The knowledge gained regarding MPTP has resulted in part in an environmental theory of disease causation. An interesting case was a chemist who developed Pd while working with MPTP.

The only possible means of contamination were through the skin or by inhaling the vapour. While it may be considered coincidental, several other cases have since been reported, suggesting that MPTP does not need to be injected to have an effect on the substantia nigra.

The preliminary finding concerning MPTP and its relationship to Pd has added another dimension to the study of the disease. Although MPTP is not the cause of Idiopathic Pd, it does suggest a chemical basis for the disease which may lead to further discoveries in this area.

Drug-induced Parkinsonism

The onset of drug-induced Parkinsonism is more rapid than that of Idiopathic Pd, and the symptoms will subside over a period of several weeks if these drugs are withdrawn.

Commonly used drugs which may induce Parkinsonism symptoms include Serenace® (haloperidol), Stemetil® (prochlorperazine), Maxolon® (metoclopramide), Neulactil® (pericyazine) and Risperidal® (risperidone).

In addition to causing Parkinsonian symptoms these medications will worsen the symptoms of a person diagnosed with Pd. This is due to the dopamine blocking action of these medications (see Information Sheet 1.4).

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